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LAHIVE & COCKFIELD, LLP
FLOOR 30, SUITE 3000
ONE POST OFFICE SQUARE
BOSTON, MA 02109

EXAMINER	
HILL, KEVIN KAI	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,402	GLIMCHER ET AL.	
	Examiner	Art Unit	
	KEVIN K. HILL	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,5,8-11,13-17 and 55-67* is/are pending in the application.

4a) Of the above claim(s) *4,5,8-10,12,14,15,56,59,60,62-65 and 67* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,11,13,16,17,55,57,58,61 and 66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *June 11, 2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Election/Restrictions

Applicant's response to the Requirement for Restriction, filed on July 22, 2009 is acknowledged.

Applicant has elected the invention of Group I, Claims 2-5 and 11-17, drawn to a method for identifying a compound which modulates an interaction between a first and a second polypeptide, the method comprising contacting *in vitro* a non-transgenic cell having a first polypeptide comprising a binding portion of a KRC polypeptide and a second polypeptide comprising a binding portion of a polypeptide selected from the group consisting of GATA3, SMAD or Runx2, classified in class 435, subclass 4.

Within Group I, Applicant has elected the following species, wherein:

i) Claims 1 and 22 are generic to the host cell is a mouse T cell;

ii) determination method steps from the lists recited in claims 9-11 and 13-15, is co-immunoprecipitation (Claim 11);

iii) second polypeptide indicator recited in Claims 1, 4-5 and 22 is GATA3; and

iv) biological activity species that is to be measured from the list recited in Claims 13, 19 and 21 is Th2 cell differentiation.

Election of Applicant's invention(s) was made with traverse.

Applicant argues that all the claims are directed to *in vitro* methods and that the Groups I-IV have the same mode of operation, function and effect, to wit, structural components, more specifically, the starting materials KRC and a polypeptide selected from the group consisting of GATA3, SMAD or Runx2.

Applicants' arguments have been fully considered but is unpersuasive. In the instant case, the inventions as claimed have materially different designs, modes of operations and effects, as evidenced by the substitute specification disclosing that the contacting step may be performed *in vitro* or *in vivo*, which is, by definition a different design, and the cell may be a transgenic or non-transgenic cell, which is, by definition a different mode of operation. Furthermore,

Applicant has provided no evidence of record that the means by which KRC interacts with GATA3, i.e. the functional protein motif, is the same motif conferring an interaction between KRC and SMAD and/or Runx2. Thus, absent evidence to the contrary, such interactions are also considered different modes of operation. Even further, Applicant has entered new claims drawn to heterologous reporter molecules, thereby evidencing the methods have distinctly different designs and effects.

Applicant argues that it would not be an undue burden on the Examiner to search all the claims, directed to *in vitro* and *in vivo* methods assayed in non-transgenic and transgenic cells/organisms, would be nearly, if not completely, co-extensive.

Applicants' arguments have been fully considered but are not found persuasive. MPEP §803 states that "If the search and examination of all the claims in an application can be made without serious burden, the examiner must examine them on the merits, even though they include claims to independent or distinct inventions."

In the instant case, a serious burden exists since each limitation, directed to a multitude of distinctly different transgenes encoding a multitude of distinctly different polypeptides, requires a separate, divergent, and non co-extensive search and examination of the patent and non-patent literature. For instance, a search and consideration of the prior art as it relates to assays performed *in vitro* with non-transgenic host cells would not be adequate to uncover prior art related to assays performed *in vivo* with transgenic animals.

Further, a search and examination of all the claims directed to all such embodiments involves different considerations of novelty, obviousness, written description, and enablement for each claim. In view of these requirements, it is the Examiner's position that searching and examining all of the claims including limitations to *in vitro* and *in vivo* methods assayed in non-transgenic and transgenic cells/organisms in the same application presents a serious burden on the Examiner for the reasons given above and in the previous Restriction Requirement.

It is noted that should Applicant traverse the species election requirement, that Applicant was invited to submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. Applicant has not done so.

The requirement is still deemed proper and is therefore made FINAL.

Applicant has requested clarification on the record as to why the Examiner did not refer to Claims 24-45 in the Requirement for Restriction mailed January 30, 2009.

The Examiner respectfully reminds Applicant that in the amendments to the Claims, papers filed May 3, 2006, Applicant had cancelled Claims 3 and 24-45. The Examiner acknowledges the typographical error failing to omit cancelled Claim 3 per the claims of Groups I-IV.

Amendments

In the reply filed July 22, 2009, Applicant has cancelled Claims 2-3, 6-7, 18-54, amended Claims 1 and 13-15, and added new claims, Claims 55-67.

Claims 4-5 are drawn to non-elected second polypeptide species.

Claims 8-10 and 67 are drawn to non-elected non-transgenic host cell species.

Claims 12 and 14-15 are drawn to non-elected determination method step species.

Claim 56 recites a cDNA molecule (SEQ ID NO:1), and thus is a transgenic nucleic acid molecule that properly belongs to Group II.

Claims 59-60 and 63-65 are drawn to non-elected transgenic host cells, per the recitation of a reporter gene which is an art-recognized heterologous nucleic acid construct (pg 30, lines 8-10, 22-26), that properly belong to Group II.

Claim 62 is drawn to a non-elected cytokine species.

Claims 4-5, 8-10, 12, 14-15, 56, 59-60, 62-65 and 67 are pending but withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected invention, there being no allowable generic or linking claim.

Claims 1, 11, 13, 16-17, 55, 57-58, 61 and 66 are under consideration.

Priority

This application is a 371 of PCT/US04/36641 filed November 3, 2004, which is a continuation of U.S. application 10/701,401 filed November 3, 2003, which is a continuation-in-part of PCT/US02/14166 filed May 3, 2002. Applicant's claim for the benefit of a prior-filed

application parent provisional application 60/288,369 filed May 3, 2001 under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged.

Information Disclosure Statement

Applicant has filed Information Disclosure Statements on June 11, 2009 that has been considered. The signed and initialed PTO Forms 1449 are mailed with this action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 1, 11, 13, 16-17, 55, 57-58, 61 and 66 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for non-transgenic human indicator cells, does not reasonably provide enablement for an enormous genus of indicator cell types such as prokaryotic, fungal, plant, invertebrate, vertebrate, avian or mammalian cells that endogenously encode GATA3 and a human KRC polypeptide having the amino acid sequence of SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

While determining whether a specification is enabling, one considers whether the claimed invention provides sufficient guidance to make and use the claimed invention. If not, whether an artisan would have required undue experimentation to make and use the claimed invention and whether working examples have been provided. When determining whether a specification meets the enablement requirements, some of the factors that need to be analyzed are: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and whether the quantity of any necessary experimentation to make or use

the invention based on the content of the disclosure is "undue" (*In re Wands*, 858 F.2d 731, 737, 8 USPQ2ds 1400, 1404 (Fed. Cir. 1988)). Furthermore, USPTO does not have laboratory facilities to test if an invention will function as claimed when working examples are not disclosed in the specification. Therefore, enablement issues are raised and discussed based on the state of knowledge pertinent to an art at the time of the invention. And thus, skepticism raised in the enablement rejections are those raised in the art by artisans of expertise.

The Breadth of the Claims, The State of the Prior Art, and the Level of One of Ordinary Skill

People of the ordinary skill in the art will be highly educated individuals such as medical doctors, scientists, or engineers possessing advanced degrees, including M.D.'s and Ph.D.'s. Thus, these people most likely will be knowledgeable and well-read in the relevant literature and have the practical experience in formation of transcription factor complexes, GATA factors and KRC factors. Therefore, the level of ordinary skill in this art is high.

With respect to the indicator cells, the claims are broad for reasonably embracing an enormous genus of prokaryotic, fungal, plant, invertebrate and vertebrate cell types [0125]. However, the instantly elected invention is to the use of a non-transgenic cell, and thus each of the first and second polypeptides must necessarily be naturally encoded by the genomes of the indicator cell.

With respect to the second polypeptide, the art does not recognize bacteria, fungi, plants or invertebrates to endogenously encode vertebrate GATA3 required by the claims. For example, while the art recognizes invertebrates such as fruit flies (D. melanogaster) and worms (C. elegans) encode a handful of GATA factor genes in their respective genomes, the art does not recognize a one-to-one developmentally functional correspondence between the invertebrate GATA factors and the vertebrate GATA factors (Patient et al, Curr. Op. Genetics and Development 12:416-422, 2002; Lowry et al, J. Mol. Evolution 50:103-115, 2000). Although the C-terminal zinc finger and basic domain have been conserved throughout evolution, there appear to be no other conserved regions across all GATA factors. Furthermore, the evolutionary pathway of GATA factors among non-vertebrates appears to be much different from that within vertebrates. Thus, sequence comparisons do not provide convincing evidence for insect-vertebrate orthologue pairs. For this reason, the scope of the non-transgenic indicator cells

endogenously encoding GATA3 is enabled only for vertebrate cells, e.g. avian, murine and/or human cells, because the art recognizes the genomes of avian, murine and human organisms to naturally encode GATA3.

With respect to claims directed to Th2 cytokine production, those of ordinary skill in the art recognize that prokaryotic, fungal, plant and invertebrate cell types are biologically incapable of developing Th2 cells, and thus Th2 cytokine production. For this reason, the scope of the non-transgenic indicator cells is enabled only for vertebrate cells, e.g. avian, murine and/or human cells because the art recognizes avian, murine and human organisms to produce Th2 cells capable of producing Th2 cytokines.

With respect to a human KRC polypeptide encoded by the indicator cell, "a claim in a dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers". See MPEP §2164.08. However, those of ordinary skill in the art immediately recognize that it is axiomatic that only human cells naturally encode the human KRC polypeptide having the amino acid sequence of SEQ ID NO:2. For this reason, the scope of the non-transgenic indicator cells is enabled only for human cells.

The specification fails to provide any guidance as to how an artisan would have dealt with the art-recognized, limitations of the claimed method commensurate with the scope of the claimed invention and therefore, limiting the claimed invention to non-transgenic human indicator cells cultured *in vitro*, is proper.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

2. Claims 1, 11, 16-17, 55, 57-58 and 66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Emerson (U.S. 2002/0022021) in view of Haenlin et al (Genes and Develop. 11:3096-3108, 1997), Matthews et al (Eur. J. Biochem. 267:1030-1038, 2000), Cubbada et al (Genes and Develop. 11:3083-3095, 1997), (Arora et al, Cell 81:781-790, 1995; *of record in IDS), Wu et al (Genomics 35:415-424, 1996; *of record in IDS), Hicar et al (Genomics 71:89-100, 2001; *of record in IDS) and Ting et al (Nature 384(6608):474-478, 1996).

Determining the scope and contents of the prior art.

Emerson discloses a method for identifying a compound which modulates [0045] an interaction between a first polypeptide and a second polypeptide, specifically a protein complex comprising a zinc-finger GATA-1 protein [0016-22] the method comprising the steps of:

a) providing an indicator composition comprising a cell, e.g. mammalian cell [0093, 0098], cultured *in vitro*,

b) contacting the indicator composition with a member of a library of test compounds [0046], and

c) selecting from the library of test compounds a compound of interest that modulates the ability of the first and second polypeptide to interact as compared to an appropriate control to thereby identify a compound which modulates an interaction between a first and second polypeptide [0095-96], wherein determining the ability of the test compound to modulate the interaction of the first polypeptide and the second polypeptide comprises determining the ability of the test compound to modulate the coimmunoprecipitation of the first polypeptide and the second polypeptide [0094].

Emerson does not disclose the physical interaction between a GATA factor and another zinc-finger protein comprising a CCHC zinc-finger motif. However, at the time of the invention, Haenlin et al taught the physical interaction between a GATA-1-like factor, Pannier, and a zinc-finger protein, Ush. Matthews et al taught that the topology of CCHC zinc-fingers, present in Ush, is essential for GATA-binding.

Neither Emerson, Haenlin et al nor Matthews et al teach a KRC polypeptide. However, at the time of the invention, Cubbada et al taught that Drosophila Shn, an art-recognized KRC-like polypeptide (Arora et al, 1995; Wu et al, 1996) comprises structurally related zinc-finger motifs as in Ush, specifically a CCHC zinc finger (pg 3090, Figure 6). Wu et al taught the cloning of KRC from murine thymocytes (Figure 3) and the identification of KRC homologs in humans and rat (Figure 6), wherein said mammalian KRC polypeptides comprise a CCHC zinc finger motif (Figure 4). Similarly, Hicar et al taught the cloning and characterization of human HIVEP3, also known in the art as human KRC, wherein said human KRC has an amino acid sequence 100% identical to SEQ ID NO:2 (sequence alignment results available in SCORE), wherein said human KRC comprises a CCHC zinc finger motif (Figure 3; amino acids 645-666 of SEQ ID NO:2) and is expressed in thymocytes.

Neither Emerson, Haenlin et al, Matthews et al, Cubbada et al, Wu et al nor Hicar et al teach the expression of GATA-3 in thymocytes. However, at the time of the invention, Ting et al taught that GATA-3 is expressed in thymocytes and T cells.

Ascertaining the differences between the prior art and the claims at issue, and Resolving the level of ordinary skill in the pertinent art.

People of the ordinary skill in the art will be highly educated individuals such as medical doctors, scientists, or engineers possessing advanced degrees, including M.D.'s and Ph.D.'s. Thus, these people most likely will be knowledgeable and well-read in the relevant literature and have the practical experience in formation of transcription factor complexes, GATA factors and KRC factors. Therefore, the level of ordinary skill in this art is high.

"A person of ordinary skill in the art is also a person of ordinary creativity, not an automaton." *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, ___, 82 USPQ2d 1385, 1397 (2007). "[I]n many cases a person of ordinary skill will be able to fit the teachings of multiple patents together like pieces of a puzzle." *Id.* Office personnel may also take into account "the inferences and creative steps that a person of ordinary skill in the art would employ." *Id.* at ___, 82 USPQ2d at 1396.

Those of ordinary skill in the art recognize that vertebrate cells naturally encode and express c-Jun and/or c-Fos polypeptides.

Considering objective evidence present in the application indicating obviousness or nonobviousness.

The person of ordinary skill in the art is a hypothetical person who is presumed to have known the relevant art at the time of the invention. Factors that may be considered in determining the level of ordinary skill in the art may include: (1) "type of problems encountered in the art;" (2) "prior art solutions to those problems;" (3) "rapidity with which innovations are made;" (4) "sophistication of the technology; and" (5) "educational level of active workers in the field. In a given case, every factor may not be present, and one or more factors may predominate." *In re GPAC*, 57 F.3d 1573, 1579, 35 USPQ2d 1116, 1121 (Fed. Cir. 1995); *Custom Accessories, Inc. v. Jeffrey-Allan Industries, Inc.*, 807 F.2d 955, 962, 1 USPQ2d 1196,

1201 (Fed. Cir. 1986); *Environmental Designs, Ltd. V. Union Oil Co.*, 713 F.2d 693, 696, 218 USPQ 865, 868 (Fed. Cir. 1983).

The combination of prior art cited above satisfies the factual inquiries as set forth in *Graham v. John Deere Co.*, 383 U.S. 1,148 USPQ 459 (1966). Once this has been accomplished the holdings in KSR can be applied (*KSR Intemational Co. v. Teleflex Inc.* (KSR), 550 U.S., 82 USPQ2d 1385 (2007): "Exemplary rationales that may support a conclusion of obviousness include: (F) Known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art.

It would have been obvious to one of ordinary skill in the art to assay a first polypeptide comprising a KRC polypeptide and a second polypeptide comprising a GATA3 polypeptide in a method for identifying a compound which modulates an interaction between a first polypeptide and a second polypeptide because the design incentives provided a reason to make such an adaptation, the invention resulted from application of the prior knowledge in a predictable manner, and "a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipate success, it is likely that product not of innovation but of ordinary skill and common sense." In the instant case, a) the prior art within the same field of endeavor as that of Applicant's invention taught a similar or analogous method to assay a first polypeptide and a second polypeptide comprising a GATA polypeptide in a method for identifying a compound which modulates an interaction between a first polypeptide and a second polypeptide (Emerson), b) there were design incentives which would have prompted adaptation of the known method, specifically the recognition of a protein-protein interaction between a GATA factor and a polypeptide comprising a CCHC motif, such as KRC (Haenlin et al, Matthews et al, Cubbada et al, Wu et al, Hicar et al), c) the differences between the claimed invention and the prior art were encompassed in known variations or in a principle known in the prior art, specifically the routinely practiced assaying of physical interactions between a first polypeptide of interest and second polypeptide of interest by those of ordinary skill in the art pursuing known options within his or her technical grasp (Emerson, Haenlin et al), d) those of ordinary skill in the art in view of the design incentives could have implemented the claimed variation of the prior art, and the claimed variation would have been predictable,

specifically in light of the topology of CCHC zinc-fingers, present in KRC and essential for GATA-binding (Matthews et al, Cubbada et al, Hicar et al), and e) GATA-3 was recognized in the prior art to be expressed in the same cell type as KRC, specifically T cells and T lymphocytes (Wu et al, Hicar et al, Ting et al).

The cited prior art meets the criteria set forth in both *Graham* and *KSR*, and the teachings of the cited prior art provide the requisite teachings and motivations with a clear, reasonable expectation of success. Thus, absent evidence to the contrary, the invention as a whole is *prima facie* obvious.

3. Claims 13 and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Emerson (U.S. 2002/0022021) in view of Haenlin et al (Genes and Develop. 11:3096-3108, 1997), Matthews et al (Eur. J. Biochem. 267:1030-1038, 2000), Cubbada et al (Genes and Develop. 11:3083-3095, 1997), (Arora et al, Cell 81:781-790, 1995; *of record in IDS), Wu et al (Genomics 35:415-424, 1996; *of record in IDS), Hicar et al (Genomics 71:89-100, 2001; *of record in IDS) and Ting et al (Nature 384(6608):474-478, 1996), as applied to Claims 1, 11, 16-17, 55, 57-58 and 66 above, and in further view of Lee et al (J. Immunol. 160:2343-2352, 1998).

Determining the scope and contents of the prior art.

Emerson discloses the method may comprise the step of determining the effect of the test compound identified as modulating the interaction between the first and second polypeptide on altering the activation of transcription in a cell [0018].

Neither Emerson, Haenlin et al, Matthews et al, Cubbada et al, Wu et al, Hicar et al nor Ting et al teach:

ii) determining the effect of the test compound identified as modulating the interaction between the first and second polypeptide on Th2 cytokine production, and

iii) wherein the Th2 cytokine is IL-4, IL-5 and/or IL-13.

However, at the time of the invention, Lee et al taught that the Th2 cytokine IL-5 gene is transcriptionally regulated by GATA-3 (pg 2349, col. 1, ¶ 2-4).

Considering objective evidence present in the application indicating obviousness or nonobviousness.

It would have been obvious to one of ordinary skill in the art to substitute a first endogenous reporter gene as taught by Emerson with a second endogenous reporter gene, more specifically the Th2 cytokine gene IL-5 as taught by Lee et al in a method for identifying a compound which modulates an interaction between a first polypeptide and a second polypeptide comprising determining the effect of the test compound identified as modulating the interaction between the first and second polypeptide on Th2 cytokine production with a reasonable expectation of success because the simple substitution of one known element for another would have yielded predictable results to one of ordinary skill in the art at the time of the invention. M.P.E.P. §2144.07 states "The selection of a known material based on its suitability for its intended use supported a *prima facie* obviousness determination in *Sinclair & Carroll Co. v. Interchemical Corp.*, 325 U.S. 327, 65 USPQ 297 (1945) When substituting equivalents known in the prior art for the same purpose, an express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. *In re Fout*, 675 F.2d 297, 213 USPQ 532 (CCPA 1982). M.P.E.P. §2144.06. In the instant case, it would be illogical in the art to use a reporter gene that is non-responsive or insensitive to a transcription factor complex of interest in an assay to measure changes in transcriptional activity. To put it another way, it is considered routine for the ordinary artisan to use a reporter gene that is recognized to be transcriptionally regulated by a transcription factor complex of interest in an assay to determine changes in transcriptional activity. IL-5 was known to be transcriptionally regulated by GATA-3. Thus, an artisan would be motivated to substitute a first endogenous reporter gene as taught by Emerson with a second endogenous reporter gene, more specifically the Th2 cytokine gene IL-5, because both GATA-3 and KRC are expressed in thymocytes and Lee et al teach that GATA-3 activity is an important transcriptional regulator of the Th2 cytokine IL-5 gene.

The cited prior art meets the criteria set forth in both *Graham* and *KSR*, and the teachings of the cited prior art provide the requisite teachings and motivations with a clear, reasonable expectation of success. Thus, absent evidence to the contrary, the invention as a whole is *prima facie* obvious.

Conclusion

4. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KEVIN K. HILL whose telephone number is (571)272-8036. The examiner can normally be reached on Monday through Friday, between 9:00am-6:00pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph T. Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kevin K. Hill/
Examiner, Art Unit 1633